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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,393	12/21/2001	Stephen Quirk	11301-1170 (44039-250928)	1033
22827	7590	06/09/2006	EXAMINER	
DORITY & MANNING, P.A. POST OFFICE BOX 1449 GREENVILLE, SC 29602-1449			SWOPE, SHERIDAN	
			ART UNIT	PAPER NUMBER
			1656	
DATE MAILED: 06/09/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No:

10/026,393

Applicant(s)

QUIRK ET AL.

Examiner

Sheridan L. Swope

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 08 May 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 82-96 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 82-96 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's Request for Continuing Examination, filed May 8, 2006, in response to the Final Rejection, mailed December 5, 2006, is acknowledged. It is acknowledged that Applicants have cancelled Claims 62-81 and added Claims 82-96. New Claims 82-96 are directed to a single invention, drawn to a method for detecting a plurality of metalloproteinases. Claims 82-96 are hereby examined.

#### ***Priority***

The priority date of the instant invention is taken to be December 21, 2001, the filing date of the instant application.

#### ***Specification-Objections***

##### **Abstract**

The Abstract is objected to for the phrase "the wound", on line 7, because the phrase lacks antecedent basis. The Abstract is also objected to for the phrase "Enzymes... can be detected and treated". It is assumed that said phrase is meant to mean that patients or wounds are treated, not enzymes.

#### ***Claim Rejections - 35 USC § 112-First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

##### **Enablement**

Claim 90 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying two or more metalloproteases using two or more signal

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elements and/or capture antibodies, does not reasonably provide enablement for identifying two or more metalloproteases using the same signal element. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

The nature of the invention of Claim 90 is to simultaneously detect a plurality of metalloproteases in a patient sample to a plurality of target antibodies, which specifically recognize each metalloprotease, and then detecting binding of the antibodies to the metalloproteases via a single signal element that binds all antibodies. The scope of the recited invention encompasses a method of using the same signal element, wherein the metalloproteases in the sample are not initially separated. A person of ordinary skill in the art would know that one would not be able to differentiate between any of the possible metalloproteases in the sample if all metalloproteases are detected using the same signal element unless the metalloproteases are

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first separated. Neither the specification nor the prior art provide sufficient guidance to enable the skilled artisan to make and use the recited invention. For these reasons, Claim 90 is rejected under 35 U.S.C. 112, first paragraph, for lack of enablement.

### **Written Description**

Claim 90 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. This claim is directed to a genus of methods to simultaneously detect a plurality of metalloproteases in a patient sample to a plurality of target antibodies, which specifically recognize each metalloprotease, and then detecting binding of the antibodies to the metalloproteases via a single signal element that binds all antibodies. The specification teaches the structure of no representative species of such methods. Moreover, by introducing the limitation of “wherein the first signal element and the second signal element are the same”, Claim 90 introduces New Matter because the specification fails to describe said limitation. Thus, Claim 90 is rejected under 35 U.S.C. 112, first paragraph, for insufficient written description including the introduction of New Matter.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 82-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Sodek, 1992. As described in the non-final rejection of July 7, 2004, the final rejection of January 26, 2005, the non-final rejection of May 25, 2005, and the final rejection of December 5, 2005, Sorsa et al teach a method for detecting, in a sample of fluid from a chronic, periodontal wound, the matrix metalloproteinase-8 (MMP-8). The method of Sorsa et al uses an immuno-chromatographic lateral flow technique. A first target antibody to MMP-8 is coated onto particles and acts a label that can be detected, for example, by its fluorescent or chemiluminescent properties. The target label can be attached directly to the antibody (col 14, parag 4). In the method of Sorsa et al, a sample of gingival crevicular fluid from a patient with periodontal disease is applied to a reservoir of a capillary support/absorbent membrane system. The label/target antibody/particles, which are applied to the membrane, migrate by diffusion coming in contact with and binding any MMP-8 in the sample. Further diffusion of the label/target antibody/particle/MMP-8 complex brings the complex into contact with a second capture antibody that has been attached in a zone-like reaction site within the membrane. When the liquid flow carrying the complex migrates through this zone, label/target antibody/particle complexes that contain MMP-8 are bound to the reaction site zone via the capture antibody. Thus, the zone is detected if MMP-8 is present in the sample (Abstract; col 22, lines 19-45). A person of ordinary skill in the art would know that, since the process of migration occurs by diffusion, at the end of the membrane there is an area that collects buffer and reactants not bound to the reaction zone. The method of Sorsa et al uses antibodies that specifically recognize the active or proform of MMP-8 (col 10, parag 3; col 14, parag 4-5).

Sorsa et al do not teach a method for simultaneously detecting a plurality of metalloproteinases in a sample. Rowe et al teach a method for detecting a plurality of proteins in a mixed sample using an array of capture antibodies specific for three different proteins. After incubation with the mixed sample, the binding of each specific protein to its respective capture antibody is detected by a fluorescently-labeled target antibody, which binds to the same specific protein. In this manner, the presence of each of a plurality of proteins in a mixed sample is detected (Fig 4). It would have been obvious to a person of ordinary skill in the art to incorporate the array approach of Rowe et al into the methods of Sorsa et al. In such a combined method, a sample of gingival crevicular fluid from a patient with periodontal disease comprising a plurality of metalloproteases, for example a combination of MMP-1, MMP-2, MMP-3, MMP-8, and/or MMP-9, would be reacted with particle-bound fluorescent or chemiluminescent target antibodies specific for each protease. Then diffusion of the label/target antibody/particle/metalloprotease complex would bring the complex into contact with an array of second, protease-specific capture antibodies, allowing detection of each specific metalloproteinase. Motivation to do so is derived from the fact that metalloproteases are involved in periodontal disease (Sodek et al, 1992; Abstract, Figs 2 & 3) and the array would support efficient determination of which proteases are present in patient samples and allow a treatment plan to be devised. Therefore, Claims 82-96 are rejected under 35 USC 103(a) as being unpatentable over the combination of Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Sodek et al, 1992.

In anticipation of the instant rejection, Applicants provide the following arguments to support their request that said rejection be withdrawn. None of the cited references disclose or

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suggest a method for simultaneously detecting a plurality of metalloproteinases. Sorsa et al teach the detection of only a single metalloproteinase, Sodek et al describes the role of metalloproteinases in periodontal disease, while Rowe et al discloses an array biosensor for simultaneously detecting the presence of different classes proteins in a mixture.

These arguments are not found to be persuasive for the following reasons. It is acknowledged that none of the cited references disclose or suggest a method for simultaneously detecting a plurality of metalloproteinases. Because this is a rejection under 35USC 103(a), none of the references are required to make said disclosure. As acknowledged by Applicants in their instant argument, the combination of Sorsa et al and Rowe et al provide all of the elements found in the recited invention. Thus, Sorsa et al teach a method for detecting the presence of a single metalloproteinase in a patient sample, while Rowe et al teach a an array for simultaneously detecting the presence of different proteins in a mixture. As also acknowledged by Applicants, Sodek et al provide motivation because they teach that numerous metalloproteinases are involved in wound progression and healing. MPEP 2143.01 [R-2] states that, "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." Based on the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art, there is motivation to combine the teachings of Sorsa et al, 1998, Rowe et al, 1999, and Sodek, 1992 to render obvious the instant invention.

#### **Final Comments**

It is noted that the rejection of Claims 82-96 under 35 U.S.C. 103(a) as being unpatentable over Sorsa et al, 1998 in view of Rowe et al, 1999 and further in view of Sodek,



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1992 is based on the same grounds as those explained in the Final Rejection of December 5, 2005 (pg 8-9) for the rejection of Claims 79-81 and essentially the same grounds as those explained in the First Action on the Merits of July 7, 2004 for the rejection of Claim 23.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action.

Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943.

The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.  
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SHERIDAN SWOPE, PH.D.  
PRIMARY EXAMINER